

The Office Action contends that WO/9933485 teaches each aspect of the invention of claims 8-11, 13-21, and 36-44 with the exception of the limitation that the method of screening taught in WO/9933485 does not use an antibody that specifically binds to unprocessed VEGF-D. The Office Action contends that Achen *et al* cures this deficiency. Applicants respectfully disagree.

Applicants respectfully submit that Achen *et al* was not published until after the earliest priority date of the present application. The instant application claims priority to provisional application 60/186,361, filed March 2, 2000. Achen *et al* was published in May of 2000. Moreover, to the extent that the portions of Achen *et al* on which the Office Action relies represent the work of the two inventors of the instant application, and not the work of their co-authors, Achen *et al* is not prior art to the March 2, 2001 grandparent application of the instant application because it does not represent the work of another and it was not published more than one year before the filing date of the application. Thus, Achen *et al* is not prior art.

In light of the above, Applicants maintain that the instant inventors have shown that expression of *full-length* (i.e. unprocessed) VEGF-D in the tumors led to faster tumor growth than for tumors not expressing VEGF-D or expressing only processed VEGF-D; and that tumors expressing full-length VEGF-D had more blood vessels and lymphatic vessels than tumors that did not express VEGF-D or expressing only processed VEGF-D. Most importantly, tumors expressing VEGF-D exhibited much more metastatic spread to lymph nodes than those not expressing VEGF-D or expressing only processed VEGF-D. The

claimed methods are based on these novel discoveries. The claims recite that the detection is based on specific assaying of the unprocessed VEGF-D level. Because the prior art does not teach or even suggest the surprising effect of unprocessed VEGF-D as compared to the processed VEGF-D, applicants respectfully submit that the claim rejections over the prior art under 35 U.S.C. § 103(a) have been rendered moot.

Claims 8, 12, and 22-27 stand rejected under 35 U.S.C. under 35 U.S.C. 103(a) for allegedly being unpatentable over WO/9933485 in view of Achen *et al* and Valtola *et al* or Salven *et al* or Tsurusaki *et al*.

As discussed above, applicants respectfully submit that Achen *et al* is not a prior art reference. Applicants further submit that without Achen *et al* the combination of references does not teach specific assaying of unprocessed VEGF-D level. Further, the Office Action relies on Achen *et al* to provide the motivation that one of ordinary skill in the art would need to combine the cited references. Without Achen *et al*, the Office Action does not provide any additional motivation to combine the references. As such, applicants respectfully submit that the claim rejections over the prior art under 35 U.S.C. § 103(a) have been obviated.

If there are any questions regarding this response or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and

please charge any deficiency in fees or credit any overpayments to Deposit
Account No. 05-1323 (Docket # 029065.48666C1

Respectfully submitted,

June 15, 2006


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